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Graham [GB/GB]; 436 Cambridge Science Park, Milton
Road, Cambridge CB4 0QA (GB).

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(74) Agent: **HUTCHINS, Michael, Richard**; M.R. Hutchins
& Co., 33 Connaught Way, Tunbridge Wells, Kent TN4
9QP (GB).

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(71) Applicant (*for all designated States except US*): **ASTEX
TECHNOLOGY LIMITED** [GB/GB]; 436 Cambridge
Science Park, Milton Road, Cambridge CB4 0QA (GB).

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(72) Inventors; and

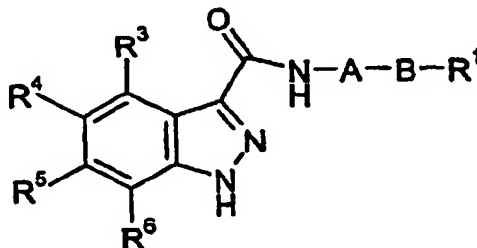
(75) Inventors/Applicants (*for US only*): **BERDINI, Valerio**
[IT/GB]; 436 Cambridge Science Park, Milton Road, Cam-
bridge CB4 0QA (GB). **PADOVA, Alessandro** [IT/IT];
Viale Don Pasquino Borghi 150, I-00144, Roma (IT).
SAXTY, Gordon [GB/GB]; 436 Cambridge Science Park,
Milton Road, Cambridge CB4 0QA (GB). **WOOLFORD,**
Allison, Jo-Anne [GB/GB]; 436 Cambridge Science Park,
Milton Road, Cambridge CB4 0QA (GB). **WYATT, Paul,**

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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: 1H-INDAZOLE-3-CARBOXAMIDE COMPOUNDS AS CYCLIN DEPENDENT KINASES (CDK) INHIBITORS.



(I)

(57) Abstract: The invention provides a compound of the formula (I) for use in the prophylaxis or treatment of a disease state or condition mediated by a cyclin dependent kinase: wherein A is a group R² or CH₂-R² where R² is a carbocyclic or heterocyclic group having from 3 to 12 ring members; B is a bond or an acyclic linker group having a linking chain length of up to 3 atoms selected from C, N, S and O; R¹ is hydrogen or a group selected from SO₂R⁸, SO₂NR⁷R⁸, CONR⁷R⁸, NR⁷R⁹ and carbocyclic and heterocyclic groups having from 3 to 7 ring members; R³, to R⁹ are defined in the description but excluding the compounds N-[(morpholin-4-yl)phenyl]-1H-indazole-3-carboxamide and N-[4-(acetaminosulphonyl)phenyl]-1H-indazole-3-carboxamide.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D231/56 C07D403/12 C07D413/12 C07D401/12 C07D409/04
C07D413/04 C07D405/04 C07D417/04 C07D417/12 C07D405/12
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 1 074 075 A (FUJISAWA PHARMACEUTICAL CO) 28 June 1967 (1967-06-28) table 2	1-79
X	S.H. WATTERSON ET AL.: "novel amide-based inhibitors of IMPDH" BIORGANIC & MEDICINAL CHEMISTRY LETTERS , vol. 12, 2002, pages 2879-2882, XP002257181 example 4L; table 1	1-79
A	WO 01 85726 A (CHOI SEI HYUN ;CHUNG HYUN HO (KR); JEONG SHIN WU (KR); KIM JONG HY) 15 November 2001 (2001-11-15) p.19, compound (12) page 65, line 7 -page 66; claims 1,4 -/-	1-79

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Schuemacher, A

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 098290 A (PHARMACIA & UPJOHN S.P.A., ITALY) 27 December 2001 (2001-12-27) cited in the application page 3, line 16 -page 4, line 20; claim 1; example 145	1-79
A	WO 01 53268 A (AGOURON PHARMA) 26 July 2001 (2001-07-26) cited in the application claims 1,8-10	1-79
A	WO 99 30710 A (SQUIBB BRISTOL MYERS CO) 24 June 1999 (1999-06-24) claims 1,19,28,29	1-79
E	WO 03 078402 A (AVENTIS PHARMA SA ;CARRY JEAN-CHRISTOPHE (FR); CHERRIER MARIE-PIER) 25 September 2003 (2003-09-25) claims 1,19,23,26; examples 18,22,23	1-79

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/03491

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 74-78 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
GB 1074075	A	28-06-1967	DE 1545835 A1	11-12-1969
			FR 4571 M	
			SE 368209 B	24-06-1974
			US 3360515 A	26-12-1967
WO 0185726	A	15-11-2001	AU 5683401 A	20-11-2001
			CA 2408448 A1	15-11-2001
			CN 1432015 T	23-07-2003
			EP 1280802 A1	05-02-2003
			WO 0185726 A1	15-11-2001
			US 2003149034 A1	07-08-2003
WO 01098290	A	27-12-2001	US 6414013 B1	02-07-2002
			AU 8574501 A	02-01-2002
			CA 2414085 A1	27-12-2001
			WO 0198290 A2	27-12-2001
			EP 1294707 A2	26-03-2003
WO 0153268	A	26-07-2001	AU 2953901 A	31-07-2001
			BG 107011 A	30-04-2003
			BR 0107783 A	19-11-2002
			CA 2388885 A1	26-07-2001
			CN 1394205 T	29-01-2003
			EP 1250326 A2	23-10-2002
			HU 0203965 A2	28-05-2003
			JP 2003520273 T	02-07-2003
			NO 20022117 A	16-09-2002
			SK 10052002 A3	04-03-2003
			WO 0153268 A2	26-07-2001
			US 2003139463 A1	24-07-2003
			US 2002161022 A1	31-10-2002
WO 9930710	A	24-06-1999	AU 747705 B2	23-05-2002
			AU 1629799 A	05-07-1999
			CA 2314355 A1	24-06-1999
			EP 1043998 A1	18-10-2000
			JP 2002508324 T	19-03-2002
			WO 9930710 A1	24-06-1999
			US 6107305 A	22-08-2000
			ZA 9811178 A	07-06-2000
WO 03078402	A	25-09-2003	FR 2836914 A1	12-09-2003
			WO 03078402 A1	25-09-2003